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## PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

Express Mail Label No. **EL908622924US** ROBERT CRIVELLO Robert Crivello

17858 U.S. PTO  
60/550970

030504

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<input checked="" type="checkbox"/> Additional inventors are being named on the <input checked="" type="checkbox"/> separately numbered sheets attached hereto					
TITLE OF THE INVENTION (280 characters max)					
TITLE A DEVICE FOR HOLDING A COLUMN OR CARTRIDGE IN PROXIMITY TO A DETECTOR AND METHODS OF USING THE SAME					
Direct all correspondence to: CORRESPONDENCE ADDRESS					
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ENCLOSED APPLICATION PARTS (check all that apply)					
<input checked="" type="checkbox"/> Specifications, claims, abstract		9		<input type="checkbox"/> CD(s), Number <input type="text"/>	
<input checked="" type="checkbox"/> Figures		3		<input checked="" type="checkbox"/> Other: Prepaid Return Postcard	
<input type="checkbox"/>		Application Data Sheet. See 37 CFR 1.76			
METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT					
<input type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27.					
<input type="checkbox"/> A check or money order is enclosed to cover the filing fees					
<input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge filing fees or credit any overpayment to Deposit Account Number:					
				23-0503	FILING FEE AMOUNT (\$) 160.00
The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.					
<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes, the name of the U.S. Government agency and the Government contract number are:					

Respectfully submitted,

SIGNATURE

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Date

March 5, 2004

REGISTRATION NO.  
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29,809

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04-391

USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT

**Docket No. 04-391**

**PROVISIONAL APPLICATION PATENT COVER SHEET**

**SECOND PAGE**

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Docket No. 04-391

**CERTIFICATE OF MAILING BY "EXPRESS MAIL"**  
**(37 CFR § 1.10) No. EL 908622924 US**

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**TITLE OF INVENTION:**

A DEVICE FOR HOLDING A COLUMN OR CARTRIDGE IN PROXIMITY  
TO A DETECTOR AND METHODS OF USING THE SAME

**FILING DATE:** HERewith

**ASSIGNEE:** WATERS INVESTMENTS LIMITED

**APPLICATION NUMBER (if known):** UNKNOWN

**MAIL STOP- PROVISIONAL APPLICATION**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

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ROBERT CRIVELLO  
Robert Crivello

**TRANSMITTAL LETTER**

Enclosed for filing in the above identified provisional patent application are the following documents:

Provisional patent application transmittal letter (2 pgs); specifications including claims and abstract (9 pgs), formal drawings (3 pgs) and prepaid return postcard.

March 5, 2004  
Reg. No. 29,809

  
Anthony J. Jamiuk

5                   A DEVICE FOR HOLDING A COLUMN OR  
CARTRIDGE IN PROXIMITY TO A DETECTOR  
AND METHODS OF USING THE SAME

10           FIELD OF THE INVENTION

The present invention relates to analytical instruments and methods of analysis.

                  BACKGROUND OF THE INVENTION

15   The present invention relates to methods and devices for minimizing band spreading caused by long tubing runs between a separation column or cartridge and a detector. Chemical analysis is a process in which the presence and/or quantity of a composition is determined. Chromatography is a process in which compositions are separated from each other, often used in chemical analysis. Typically, samples are in the form of a solution  
20   holding one or more compositions. A pump creates a flow of fluid. Samples are placed into this flow of fluid by a sample injector. The sample is carried by the flow of fluid through tubing to a column or cartridge. The cartridge or column is packed with a solid phase media. The different compounds held in the sample exhibit different affinities for the solid phase material and separate from each other. The flow from the column is  
25   received by a detector. The detector produces a signal that changes as the properties of the fluid changes takes place over time due to the separation of the compounds. These changes are recorded as peaks or bands and are indicative of a particular composition.

30   The separation of compound by the column or cartridge is reversible. The compositions leaving the solid phase media are able to redistribute and mix with the surrounding fluid. This redistribution of the concentrated compositions is known as band spreading. Band spreading is undesirable in that it tends to obscure compositions that are present in small concentrations.

35   Columns and cartridges are often contained in an assembly with sample injector functions and pumping functions. The assembly allows the environment of the column and cartridge to be controlled. The column and/or cartridge communicate with one or more detectors through runs of tubing. The long runs of tubing promote band spreading.

40   Placement of the column and/or cartridge in close proximity to the detector is difficult. The column or cartridge is then subjected to changes in temperature which may lead to shifts in peaks. Moving the column and/or cartridge to the detector, away from the sample injector, may cause mixing of the samples with each other.

45

## SUMMARY OF THE INVENTION

Embodiments of the present invention are directed to methods and devices for minimizing band spreading of compositions separated by chromatographic processes.

5 One embodiment of the present invention features a device for holding a separation column or cartridge. The device comprises a housing having a chamber for receiving one or more columns or cartridges. The columns and cartridges have an inlet for receiving fluid and an outlet for discharging fluid and an column axis corresponding generally with the flow of fluid from the inlet to the outlet. The columns and cartridges are suitable for  
10 performing separations in which a constant temperature is desirable. The housing further comprises a heating element for maintaining said chamber at a constant temperature. The device further comprises positioning means for placing the column and cartridge outlet in proximity to a detector.

15 As used herein the term "detector" means any instrument which produces a distinctive signal in the presence of a composition. The detector is preferably selected from the group of detectors consisting of mass spectrometers; optical detectors, such as photodiode array detectors, ramon light scattering detectors, absorbance detectors, fluorescence detectors, refractometers, electro-chemical detectors, viscosity detectors and the like.

20 Preferably, the columns and cartridges receive sample from a sample injector and a fluid from a pump. A common sample injector is an autosampler. An autosampler is a apparatus for receiving samples in one or more vials or containment vessels and withdrawing aliquots of such samples. The aliquots are injected into the flow from a  
25 pump in a automatic manner. This application will use the term sample injector to encompass manual sample injectors and automatic sample injectors, i.e. autosamplers.

The positioning means comprises an arm, slide, linkage or hinge. The arm, slide, linkage or hinge are capable of movement and positioning to allow the housing to be placed with  
30 the outlet of a column or cartridge proximal to the inlet of the detector. The short distance spanning the outlet of the column and/or cartridge to the inlet of the detector is, preferably, spanned by a relatively short tube or conduit. The shorter distance improves the sensitivity of the detector, pump and sample injector combination by reducing band spreading. For example, in one embodiment where the positioning means comprises a  
35 hinge, the hinge is affixed to the pump or sample injector apparatus and the housing is swung to a position in which the outlet of the column is close to the inlet of the detector.

Preferably the first housing has a cradle. The cradle has a cradle axis of rotation substantially aligned parallel with said column axis. The cradle has a cradle opening for  
40 receiving columns and cartridges. The cradle opening has an open position and a closed position. The opening is shut upon the cradle assuming the closed position to provide a temperature controlled environment for the column or cartridge. In the open position, the opening is accessible to receive and remove columns and cartridges.

45 Preferably, the heating element is contained in the cradle. One preferred heating element is electrical resistance circuits.

Preferably, device is part of an assembly of a pump, sample injector or combined modules of pumps and sample injector. Thus, the device of the present invention is convenient for use and promotes laboratory bench organization.

5 A further embodiment of the present invention features a method of minimizing band spreading in separation processes. The method comprising the steps of providing a first housing having a chamber for receiving one or more columns or cartridges. The columns and cartridges have an inlet for receiving fluid and an outlet for discharging fluid and an  
10 column axis corresponding generally with the flow of fluid from the inlet to the outlet. The column and cartridges are for performing separations such as liquid chromatography. The housing has a heating element for maintaining the chamber at a constant temperature. The method further comprises the step of providing positioning means for placing the column and cartridge outlet in proximity to a detector to allow connection to a detector.  
15 The method comprises the step of placing the housing in proximity to the detector with the positioning means to minimize tubing spanning from the column outlet to the detector and minimize band spreading.

Preferably, the method further comprises the step of providing a device wherein the first  
20 housing has a cradle having an opening. The cradle has a cradle axis of rotation substantially aligned parallel with the column axis. The cradle rotates between an open position and a closed position. In the open position, the cradle opening is accessible for receiving columns and cartridges. The opening is shut upon the cradle assuming the closed position to provide a controlled environment for the column and/cartridge. The  
25 method further comprising the steps of rotating the cradle to the open position to receive a column or cartridge. Next, rotating the cradle to assume the closed position, and positioning the column or cartridge in proximity to the detector.

Preferably, the positioning means is an arm, linkage, slide or hinge. The positioning  
30 element is preferably attached to apparatus selected from the group consisting of a pump, sample injector or a combined module a of pump and sample injector. One preferred positioning means is a hinge affixed to the housing and the injector or pump. The housing rotated or pivots to allow positioning close to a detector.

35 Preferable the method further comprises the step of providing a heating element contained in said cradle. The method further comprises the step of heating the cradle to a constant temperature.

40 These and other features and advantages will be apparent to individuals skilled in the art upon reference to the figures and detailed description that follow.

#### BRIEF DESCRIPTION OF THE DRAWINGS

45 Figure 1 depicts a device embodying features of the present invention;

Figure 2 depicts the device positioned to cooperate with a detector;



Figure 3 depicts a device embodying features of the present invention.

## 5 DETAILED DESCRIPTION OF THE INVENTION

The present invention will be described in detail with respect to methods and devices for minimizing band spreading of compositions separated by chromatographic processes. However, individuals skilled in the art will recognize that aspects of the present invention  
10 have broader application can be used wherever it is desirable to place a separation device such as a column or cartridge close to a further instrument.

One embodiment of the present invention a device for holding a separation column or cartridge, generally designated by the numeral 11, is depicted in Figure 1 and 2. The  
15 device 11 comprises a housing 15 and positioning means 17.

Housing 15 has a chamber 19 for receiving one or more columns or cartridges (not shown) as best seen in Figure 3. Columns and cartridges are well known in the art. Columns and cartridges generally have an inlet for receiving fluid and an outlet for  
20 discharging fluid and an column axis corresponding generally with the flow of fluid from the inlet to the outlet. The columns and cartridges are suitable for performing separations in which a constant temperature is desirable.

For the purpose of this discussion, the column and/or cartridge inlet will be described as being close to the positioning means 17. And, the column and/or cartridge outlet will be  
25 described as being distal from the positioning means 17.

Positioning means 17 places the column and cartridge outlet in proximity to a detector (not shown). As used herein the term "detector" means any instrument which produces a  
30 distinctive signal in the presence of a composition. The detector is preferably selected from the group of detectors consisting of mass spectrometers; optical detectors, such as photodiode array detectors, ramon light scattering detectors, absorbance detectors, fluorescence detectors, refractometers, electro-chemical detectors, viscosity detectors and the like. It is common to place mass spectrometers to the right of a pump and sample  
35 injector assembly, as one faces the front of the pump and sample injector assembly.

Preferably, the columns and cartridges receive sample from a sample injector and a fluid from a pump. A common sample injector is an autosampler. An autosampler is a  
40 apparatus for receiving samples in one or more vials or containment vessels and withdrawing aliquots of such samples. The aliquots are injected into the flow from a pump in an automatic manner. This application will use the term sample injector to encompass manual sample injectors and automatic sample injectors, i.e. autosamplers.

The positioning means 17 comprises an arm, slide, linkage, interfitting sliding elements, such as sliding cylinders in the nature of a telescope, flexible conduit members or hinges.  
45 Positioning means 17 depicted in Figures 1 and 2, is a hinge which secures the housing to

a pump or sample injector designated by the numeral 21. Starting with Figure 1, positioning means 17 allows the housing 15 to swing outward and, moving to Figure 2, extend to the right to assume a position in from of a detector (not shown) placed to the right

5

The arm, slide, linkage, interfitting sliding elements, flexible conduit members or hinge are capable of movement and positioning to allow the housing 15 to be placed with the outlet of a column or cartridge proximal to the inlet of the detector. The short distance spanning the outlet of the column and/or cartridge to the inlet of the detector is, preferably, spanned by a relatively short tube or conduit. The shorter distance improves the sensitivity of the detector, pump and sample injector combination by reducing band spreading. For example, in one embodiment where the positioning means 17 comprises a hinge, the hinge is affixed to the pump or sample injector apparatus 21 and the housing is swung to a position in which the outlet of the column is close to the inlet of the detector.

15

Other embodiments of positioning means 17, such as arm, slide, linkage, interfitting sliding elements, flexible conduit members and the like, are well known. Thus, one end of an arm, slide, linkage, interfitting sliding elements, flexible conduit member or similar element would be attached to the pump or sample injector 21 and the other end made available for movement to a position proximal to the inlet of a detector.

20

Preferably the housing 15 has a cradle 23. The cradle 23 is rotatably attached to the housing 15 with a cradle axis of rotation substantially aligned parallel with the column axis. The cradle 23 has a cradle opening 25 for receiving columns and cartridges (not shown). The cradle opening 25 has an open position, depicted in Figure 3 and a closed position, depicted in Figure 2. The cradle opening 25 is shut upon the cradle 23 assuming the closed position to provide a temperature controlled environment for the column or cartridge. In the open position, the cradle opening 25 is accessible to receive and remove columns and cartridges.

25

Cradle 23 has slots 27a and 27b for receiving one or more tubes or conduits for placing fluid into a column or cartridge. Cradle 23 also has one or more slots 29a (only one shown) for receiving one or more tubes or conduits for removing fluid from the column or cartridge and directing such fluid into the inlet of a detector.

30

Housing 15 further comprises a heating element 21 for maintaining the chamber 19 and with greater particularity the cradle opening 25 at a constant temperature. As best seen in figure 3, the heating element 21 is contained in the cradle 23. One preferred heating element 21 is electrical resistance circuits thermostatically controlled in a manner known in the art.

35

Preferably, device 11 is part of an assembly 21 of a pump, sample injector or combined modules of pumps and sample injector. Thus, the device of the present invention is convenient for use and promotes laboratory bench organization.

40

The method of the present invention will be described with respect to the operation of the device. The invention features a method of minimizing band spreading in separation processes.

- 5 The method comprising the steps of providing a housing 15 having a chamber 19 for receiving one or more columns or cartridges. The columns and cartridges have an inlet for receiving fluid and an outlet for discharging fluid and an column axis corresponding generally with the flow of fluid from the inlet to the outlet. The column and cartridges are for performing separations such as liquid chromatography. The housing has a heating  
10 element 31 for maintaining the chamber 19 at a constant temperature. The method further comprises the step of providing positioning means 17 for placing the column and cartridge outlet in proximity to a detector to allow connection to a detector. The method comprises the step of placing the housing 15 in proximity to the detector with the positioning means 17 to minimize tubing spanning from the column outlet to the detector  
15 and minimize band spreading.

- Preferably, the method further comprises the step of providing a device 11 wherein the housing 15 has a cradle 23 having a cradle opening 25. The cradle 23 has a cradle axis of rotation substantially aligned parallel with the column axis. The cradle 23 rotates  
20 between an open position and a closed position. In the open position, the cradle opening is accessible for receiving columns and cartridges. The cradle opening 25 is shut upon the cradle 23 assuming the closed position to provide a controlled environment for the column and/cartridge. The method further comprising the steps of rotating the cradle 23 to the open position to receive a column or cartridge. Next, rotating the cradle 23 to  
25 assume the closed position, and positioning the column or cartridge in proximity to the detector.

- Thus, the present invention has been described in a manner which enables the individual skilled in the art to make and use the invention. These and other features and advantages  
30 will be apparent to individuals skilled in the art upon reference to the figures and detailed description that follow.

## CLAIMS

1. A device for holding a separation column or cartridge, comprising:
  - 5 a. a first housing having a chamber for receiving one or more columns or cartridges, said columns and cartridges having an inlet for receiving fluid and an outlet for discharging fluid and an column axis corresponding generally with the flow of fluid from said inlet to said outlet, said column and cartridges for performing separations, said housing having a heating element for maintaining said chamber at a constant temperature; and
  - 10 b. positioning means for placing said column and cartridge outlet in proximity to a detector.
2. The device of claim 1 wherein said detector is selected from the group of detectors  
15 consisting of mass spectrometers; optical detectors, such as photodiode array detectors, ramon light scattering detectors, absorbance detectors, fluorescence detectors, refractometers, electro-chemical detectors, viscosity detectors and the like.
3. The device of claim 1 wherein said first housing has a cradle, said cradle having an  
20 cradle axis of rotation substantially aligned parallel with said column axis and said cradle having an open position and a closed position upon rotation, and cradle opening for receiving said columns and cartridges, said opening shut upon said cradle assuming said closed position and said opening accessible upon said cradle assuming said open position.
- 25 4. The device of claim 3 wherein said heating element is contained in said cradle.
5. The device of claim 4 wherein said heating element is electrical resistance circuits.
6. The device of claim 1 wherein said positioning means is an arm having an attachment  
30 means for coupling to at least one of the group consisting of a pump or sample injector or combinations of a pump and a sample injector, said arm articulated to allow positioning proximal to a detector.
7. The device of claim 1 wherein said positioning means is selected from the group  
35 consisting of a slide, interfitting sliding elements, flexible conduit elements and combinations thereof having an attachment means for coupling to at least one of the group consisting of a pump or sample injector or combinations of a pump and a sample injector, said slide allowing positioning proximal to a detector.
- 40 8. The device of claim 1 wherein said positioning element is a hinge for attachment to apparatus selected from the group consisting of a pump, sample injector or combined modules of pumps and sample injector.
9. The device of claim 6, 7 or 8 further comprising an apparatus selected from the group  
45 consisting of a pump, sampler injector or a combined module of a pump and sample injector.



10. The device of claim 1 wherein positioning said outlet of said column and cartridge close to the detector minimizes band spreading.

5 11. A method of minimizing band spreading in separation processes comprising the steps of  
providing a first housing having a chamber for receiving one or more columns or  
cartridges, said columns and cartridges having an inlet for receiving fluid and an outlet  
for discharging fluid and an column axis corresponding generally with the flow of fluid  
10 from said inlet to said outlet, said column and cartridges for performing separations, said  
housing having a heating element for maintaining said chamber at a constant temperature;  
and positioning means for placing said column and cartridge outlet in proximity to a  
detector to allow connection to a detector whereby the proximity to said detector  
minimizes tubing spanning from said column outlet to said detector and minimizes band  
15 spreading.

12. The method of claim 11 wherein said detector is selected from the group of detectors  
consisting of mass spectrometers; optical detectors, such as photodiode array detectors,  
ramon light scattering detectors, absorbance detectors, fluorescence detectors,  
20 refractometers, electro-chemical detectors, viscosity detectors and the like.

13. The method of claim 11 wherein said first housing has a cradle, said cradle having an  
cradle axis of rotation substantially aligned with said column axis and said cradle having  
an open position and a closed position, and cradle opening for receiving said columns and  
25 cartridges, said opening shut upon said cradle assuming said closed position and said  
opening accessible upon said cradle assuming said open position.

14. The method of claim 11 wherein said heating element is contained in said cradle.

30 15. The method of claim 11 wherein said heating element is electrical resistance circuits.

16. The method of claim 11 wherein said positioning element is a hinge for attachment  
to apparatus selected from the group consisting of a pump, sample injector or combined  
modules of pumps and sample injector.

35 17. The method of claim 16 further comprising an apparatus selected from the group  
consisting of a pump, sample injector or a combined module of a pump and sample  
injector.

40 18. The method of claim 11 wherein said positioning means is selected from the group  
consisting of a slide, arm, linkage, interfitting sliding elements, flexible conduit elements,  
hinge or combinations thereof.

45 19 The method of claim 18 wherein said positioning means is adjusted to bring said  
outlet of said column and cartridge in close proximity to said detector.

**ABSTRACT**

Embodiments of the present invention are directed to methods and devices for minimizing band spreading of compositions separated by chromatographic processes.

- 5 One embodiment of the present invention features a device for holding a separation column or cartridge. The device comprises a housing having a chamber for receiving one or more columns or cartridges. The columns and cartridges have an inlet for receiving fluid and an outlet for discharging fluid and an column axis corresponding generally with the flow of fluid from the inlet to the outlet. The columns and cartridges are suitable for
- 10 performing separations in which a constant temperature is desirable. The housing further comprises a heating element for maintaining said chamber at a constant temperature. The device further comprises positioning means for placing the column and cartridge outlet in proximity to a detector.

2/26/2004

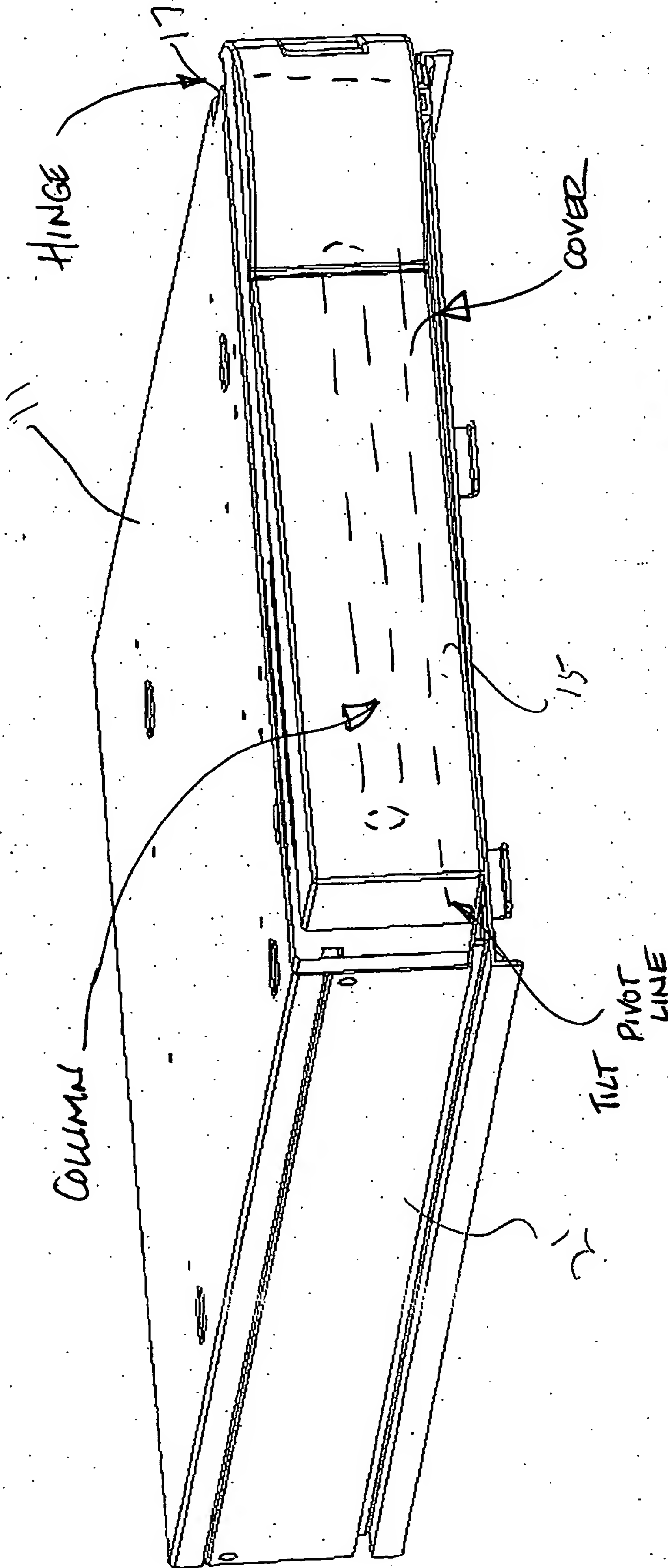
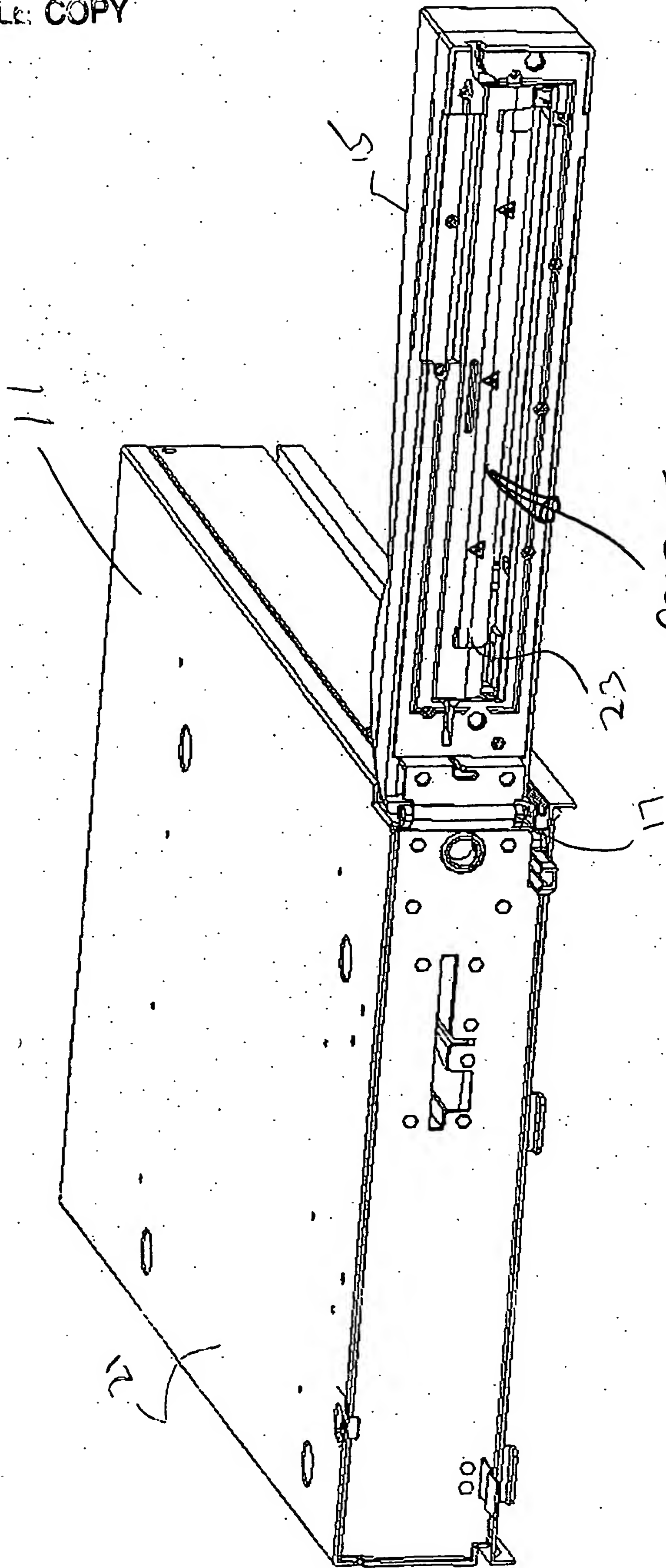
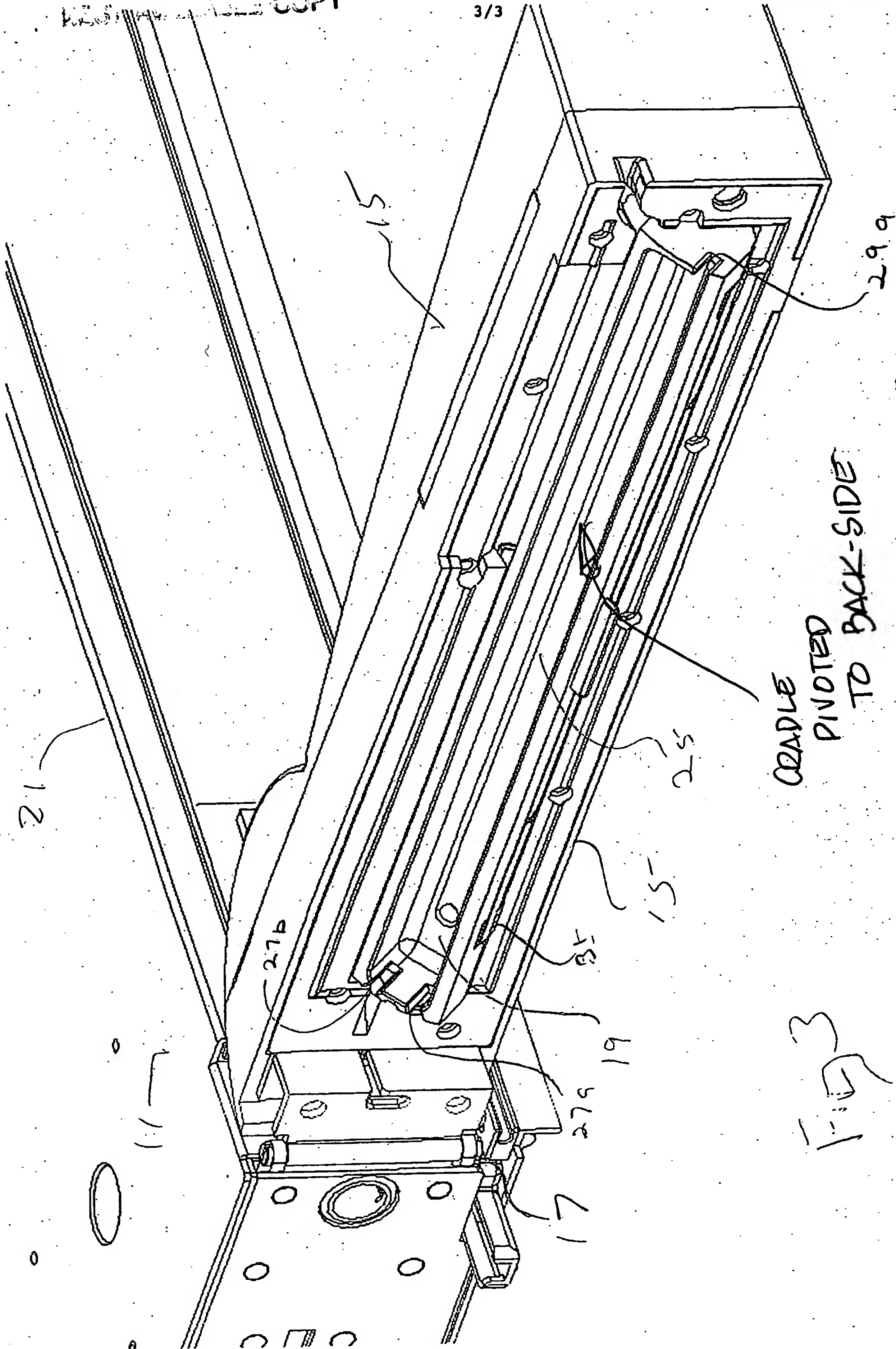


FIG 1  
COLUMN HEATER MODULE  
D. PRENTICE





2/25/2004



CRADLE  
PIVOTED  
TO BACK-SIDE  
(BACK COVER REMOVED)

FIG 3